

**REMARKS**

With entry of the present amendment claims 1, 4, 8 to 15, 18, and 22 to 43 are pending, with claims 15, 18, and 22 to 42 being withdrawn from examination by the patent office. Claim 1 has been amended to incorporate the features of original claims 2, 3, and 7. The amendments are supported by the specification and claims as filed. No new matter has been added.

This response is accompanied by a request for a one-month extension of time in which to respond to the pending office action, making the date for response February 12, 2007. The Director is hereby authorized to charge Deposit Account No. 08-2525 in the amount of \$120.00 to cover the one-month extension fee in accordance with 37 C.F.R. § 1.17(a)(1). No additional fees are believed due. However, the Director is hereby authorized to charge any deficit, or credit any overpayment, to Deposit Account No. 08-2525.

**OBJECTION OF CLAIMS 1 TO 4 AND 7 TO 9**

Claims 1 to 4 and 7 to 9 stand objected to for the use of the acronyms PDE, LF1, and UCR1 without first specifying the full term. While applicants submit that there is no requirement to include the full term in the claims and that one having ordinary skill in the art in light of the specification would know exactly what was intended by the claims as filed, the full terms have been specified in claim 1 as requested, rendering the objection moot. This amendment does not change the scope of the claims.

**REJECTION OF CLAIMS 1 TO 14 AND 43 UNDER 35 U.S.C. § 112, SECOND PARAGRAPH**

Claims 1 to 14 and 43 stand rejected under 35 U.S.C. § 112, second paragraph as vague in the recitation of the phrase “decreased aggregate formation.” Claim 1 has been amended to recite

“decreased aggregate formation as compared to native long form PDE4 polypeptide.” In view of the amendment, Applicants respectfully request reconsideration and withdrawal of this rejection.

**REJECTION OF CLAIMS 1 TO 14 AND 43 UNDER 35 U.S.C. § 112, FIRST PARAGRAPH**

Claims 1 to 14 and 43 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking written description and enablement for the full scope of the claims as filed.

Applicants respectfully traverse this rejection for the following reasons. The claims have been amended to recite a long form PDE4 polypeptide sequence with an amino-terminal deletion wherein the polypeptide sequence starts at any amino acid located between LF1 splice site and the first amino acid of the UCR1 of the native long form PDE4 polypeptide. The specification provides support for the claims as amended (*see, e.g.*, ¶ [0039]). As the sequences of the native PDE4 polypeptides are known; the lengths of the specifically claimed species are specified by position of the starting amino acid, and since a person skilled in the art knows *in vitro* methods to produce amino-terminal deletion mutants, *e.g.*, site directed mutagenesis (*see, e.g.* ¶ [0037]), applicants submit that the claims as amended are supported and enabled by the specification.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this rejection.

**REJECTION OF CLAIMS 1 TO 4 AND 10 UNDER 35 U.S.C. § 102 OVER BOLGER ET AL**

Claims 1 to 4 and 10 stand rejected under 35 U.S.C. § 102, over Bolger et al., Biochem. J., 328: 539-48 (1997). It is stated that Bolger et al. describes human PDE polypeptides including N-terminal deletions.

This rejection is traversed for the following reasons. Bolger et al. describes native PDE4D2 which lacks amino acids 1 to 78 of native PDE4D1. PDE4D2 is a native unmodified polypeptide whose N-terminal start does not lie within the region specified in claim 1, i.e., none of the five isoforms described in Bolger et al. has its N-terminal start between the LF1 splice site and the first amino acid of the UCR1 domain as required by the instant claims.

It is further noted that the statement on page 10 of the office action that “it is widely known in the art that PDE has a transmembrane region comprising 6 hydrophobic helices at the N-terminus” is incorrect. The PTO’s attention is directed to page 857 of Bolger, Cellular Signalling, 6(8): 851-859 (1994) (copy attached) which indicates under the section entitled “Subcellular localization” that it is unclear which structural features of PDE are important for membrane association and that the presence of transmembrane domains has not been demonstrated.

As the reference does not teach each and every claim limitation, Applicant’s submit that the instant claims as amended are not anticipated by Bolger et al. For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this rejection.

**REJECTION OF CLAIMS 5 TO 7 UNDER 35 U.S.C. § 103, OVER BOLGER ET AL. IN VIEW OF SHAKUR ET AL.**

Claims 5 to 7 stand rejected under 35 U.S.C. § 103 as obvious over Bolger et al. in view of Shakur et al. In making this rejection, Bolger et al. is cited for the reasons provided in the § 102 rejection and Shakur et al. is cited as describing a PDE protein in which the first 25 N-terminal amino acids have been deleted.

Applicants respectfully traverse this rejection for the following reasons. As noted above, Bolger et al. fails to describe or suggest a PDE4 polypeptide having its N-terminal start between the LF1 splice site and the first amino acid of the UCR1 domain as required by the instant claims.

Shakur et al. describe a PDE which has its first 25 N-terminal amino acids deleted (Met<sup>26</sup>-RDI). Figure 2 of the attached Bolger reference, Cellular Signalling, 6(8): 851-859 (1994), shows that Met<sup>26</sup>-RDI does not have its N-terminal start between the LF1 splice site and the first amino acid of the UCR1 domain. Thus, Shakur et al. does not overcome the deficiency of Bolger et al., and the combination of Bolger et al. and Shakur et al. cannot render the instant claims obvious.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this rejection.

**REJECTION OF CLAIMS 11 TO 13 UNDER 35 U.S.C. § 103, OVER BOLGER ET AL. IN VIEW OF  
MACKENZIE ET AL.**

Claims 11 to 13 stand rejected under 35 U.S.C. § 103 as obvious over Bolger et al. in view of MacKenzie et al. In making this rejection, Bolger et al. is cited for the reasons provided in the § 102 rejection and MacKenzie et al. is cited as describing a Ser54 mutation.

Applicants respectfully traverse this rejection for the following reasons. As noted above, Bolger et al. fails to describe or suggest a PDE4 polypeptide having its N-terminal start between the LF1 splice site and the first amino acid of the UCR1 domain as required by the instant claims. MacKenzie et al. describes native PDE4D3 polypeptides in which the serine atom at position 54 is mutated to alanine. However, MacKenzie does not describe or suggest PDE4 polypeptides having the N-terminus between the LF1 splice site and the first amino acid of the UCR1 domain. Thus, MacKenzie et al. does not overcome the deficiency of Bolger et al., and the combination of Bolger et al. and MacKenzie et al. cannot render the instant claims obvious.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this rejection.

**REJECTION OF CLAIM 14 UNDER 35 U.S.C. § 103, OVER BOLGER ET AL. IN VIEW OF BIFULCO ET AL.**

Claim 14 stands rejected under 35 U.S.C. § 103 as obvious over Bolger et al. in view of Bifulco et al. In making this rejection, Bolger et al. is cited for the reasons provided in the § 102 rejection and Bifulco et al. is cited as describing a cAMP-specific phosphodiesterase associated with tubulin through the C-terminal region of PDE.

Applicants respectfully traverse this rejection for the following reasons. Claim 14 depends from and contains all of the features of claim 1. As noted above, Bolger et al. fails to describe or suggest a PDE4 polypeptide having its N-terminal start between the LF1 splice site and the first amino acid of the UCR1 domain as required by the instant claims. Bifulco et al. also does not describe or suggest PDE4 polypeptides having the N-terminus between the LF1 splice site and the first amino acid of the UCR1 domain. Thus, Bifulco et al. does not overcome the deficiency of Bolger et al., and the combination of Bolger et al. and Bifulco et al. cannot render the instant claims obvious.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this rejection.

**REJECTION OF CLAIM 43 UNDER 35 U.S.C. § 103, OVER BOLGER ET AL. IN VIEW OF LEE ET AL.**

Claim 43 stands rejected under 35 U.S.C. § 103 as obvious over Bolger et al. in view of Lee et al. In making this rejection, Bolger et al. is cited for the reasons provided in the § 102 rejection and Lee et al. is cited as describing a crystalline structure of cAMP specific phosphodiesterase, specifically isoform PDE4D.

Applicants respectfully traverse this rejection for the following reasons. As noted above, Bolger et al. fails to describe or suggest a PDE4 polypeptide having its N-terminal start between the

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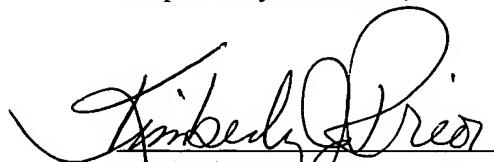
LF1 splice site and the first amino acid of the UCR1 domain as required by the instant claims. Lee et al. also does not describe or suggest PDE4 polypeptides having the N-terminus between the LF1 splice site and the first amino acid of the UCR1 domain, crystalline or otherwise. Thus, Lee et al. does not overcome the deficiency of Bolger et al., and the combination of Bolger et al. and Lee et al. cannot render the instant claims obvious.

For at least these reasons, Applicants respectfully request reconsideration and withdrawal of this rejection.

The foregoing amendment is fully responsive to the Office Action issued October 12, 2006. Applicants submit that Claims 1, 4, 8 to 15, and 22 to 43 are allowable. Early and favorable consideration is earnestly solicited.

If the Examiner believes there are other issues that can be resolved by telephone interview, or that there are any informalities remaining in the application which may be corrected by Examiner's Amendment, a telephone call to the undersigned attorney is respectfully solicited.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Kimberly J. Prior", written over a horizontal line.

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